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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,505	10/14/2004	Roger John Watling	62302(70403)	4189
21874	7590	04/23/2008		
EDWARDS ANGELL PALMER & DODGE LLP			EXAMINER	
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BOSTON, MA 02205				
		ART UNIT	PAPER NUMBER	
		4112		
		MAIL DATE	DELIVERY MODE	
		04/23/2008	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/511,505

**Applicant(s)**

WATLING ET AL.

**Examiner**

BRYAN T. KILPATRICK

**Art Unit**

4112

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 14, 17-25 and 37 is/are rejected.
- 7) ☒ Claim(s) 6-13, 15, 16 and 26-36 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 October 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 10/14/2004.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Summary***

1. This is the initial Office action based on the 10/511,505 application having the international filing date April 16, 2003
2. Claims 1-37 are pending.

### ***Specification***

3. The disclosure is objected to because of the following informalities: the use of the word "ionized" on page 15, line 14 of the Specification. The current application has used the spelling as well as variations of the word "ionised." through out the application; the applicant must maintain consistency of the language used in the current application.

Appropriate correction is required.

4. The use of the trademark Perspex on page 35, line 25 of the Specification section has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Objections***

5. Claims 6-13, 15-16, and 26-36 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim 4. See MPEP § 608.01(n). Accordingly, the claims 6-13, 15-16, and 26-36 have not been further treated on the merits.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,777,324 (HILLENKAMP), as evidenced by W.O. 00/47236 (BABICH ET AL.), and evidenced by Mass Spectrometry, Principles and Applications; 2nd Edition (DE HOFFMANN ET AL.).

In claim 1, column 10 of HILLENKAMP, the mixing of a sample comprised of a major portion of matrix material and a minor portion of analyte which are then deposited on a support is taught. Although HILLENKAMP does not expressly teach the use of matrices to immobilize a sample to a support, section 5.3, first paragraph of the Specification of BABICH ET AL. cites a reference for the use of matrices to immobilize samples to solid supports (Handbook of Enzyme Biotechnology, 2<sup>nd</sup> Edition, Wiseman, 1985). Additionally, in subsection 2 -

Practical considerations, of section 1.6 - Laser Desorption and Matrix-assisted Laser Desorption Ionization, of DE HOFFMANN ET AL. on page 31, criteria for matrix material is taught; with one of the criteria being matrices that "lack chemical reactivity" which suggest the matrix is inert.

8. Claims 1 – 3 are rejected under 35 U.S.C. 102(b) as being anticipated by "Sugar additives for MALDI matrices improve signal allowing the smallest nucleotide change (A:T) in a DNA sequence to be resolved" by SHAHGOLI ET AL.

With respect to claim 1, SHAHGOLI ET AL. teaches sugar additives for MALDI matrices (abstract) which are affixed to a support (page 3, column 2, lines 1-12). Although SHAHGOLI ET AL. does not explicitly state the matrices taught therein are inert, one of ordinary skill in the art would know a matrix is inherently inert so that there is no interaction between the matrix and sample mixed therein.

With respect to claim 2, SHAHGOLI ET AL. teaches on page 2, that the use of glucose as a matrix in mass spectrometry has been studied previously. Specifically a reference is made therein to BEAVIS ET AL. ("Sample matrix effect in infrared laser neutral desorption, multiphoton-ionization mass spectrometry. *Chem. Phys. Lett.*, Vol. 146, 1988, pages 310 – 313.), wherein "BEAVIS ET AL. used sucrose and glucose as a matrix for the multi-photon ionization of dipeptides in a reflectron TOF mass spectrometer."

The examiner notes claim 3 further limits the vegetable flour of claim 1, but does not require the selection of vegetable flour as the collection matrix.

9. Claim 14 rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,179,005 (PHILLIPS ET AL.).

Figures 3 and 4 from the Drawings of PHILLIPS ET AL. present a device which meets the description set forth by the claim. The device taught has multiple layers: a clamping layer that presses another disposable layer on top of a matrix and sample, and a bottom supporting layer. The disposable and clamping layers have openings for accessing samples and/or matrices.

10. Claims 17 – 25, 37 are rejected under 35 U.S.C. 102(b) anticipated by VESTAL ET AL. (WO 96/03768).

The material stated in VESTAL ET AL. (Specification section, pages 1 – 22, and Claims section, pages 23 – 36) encompass the claimed invention of stated in claims 17 – 22 and 37 presented by the current application.

With respect to claims 17 – 22, VESTAL ET AL. teaches in claim 1 “a system for analyzing a plurality of samples” (method of detecting and method of quantifying), a laser source for striking each sample on each sample support while within the receiving chamber with a laser pulse to desorb and ionize sample molecules” (exposing the sample, internal standard, and/or elements to

high energy radiation capable of ionization) and "computer means for recording test data from the mass spectrometer for each of the plurality of samples on the sample supports as a function of the identification means" (measuring and determining the quantity of ionized sample, internal standard, and/or elements by mass spectrometry). VESTAL ET AL. teaches in claim 1, an analysis - which includes detection, identification, and quantification - of any component that is present in a sample deposited on a support by way of ionization via high energy radiation in the form of laser pulses using mass spectrometry.

Claims 17 – 20 state "method of quantifying simultaneously a plurality of elements in a fluid sample adsorbed onto or into an inert collection matrix" and claim 21 states "method of quantifying simultaneously a plurality of elements in a fluid sample adsorbed/absorbed onto or into an inert collection matrix." VESTAL ET AL. teaches the use of an "appropriate matrix" that is dictated by the sample to be analyzed in the second paragraph of the Background of Invention section, page 1.

Claim 22 states "method of quantifying simultaneously a plurality of elements in a fluid sample supported on an impermeable substrate." VESTAL ET AL. states, on page 7 in the Sample Receiving Surface section, the use of a "plate 12 of stainless steel or other suitable electrically conducting material approximately 1.5 mm thick and 50 mm wide." Although VESTAL ET AL. does not explicitly state

the 1.5 mm thick stainless steel plate is impermeable to Perspex (acrylic glass or Plexiglas™) discussed on page 35, line 25; it is the Examiner's position that a 1.5 mm thick stainless steel or other suitable electrically conducting material is inherently impermeable to Perspex.

Claims 23 – 25 are dependent on independent claims 19, 20, 21, or 22. Claims 23 – 25 limit the scope of a sample to be some form of "standard" or "certified reference material (CRM)," but are still taught by claim 1 of VESTAL ET AL. on page 23. A standard or CRM is a sample with a known outcome, but still a sample that can be considered to be part of the plurality of samples to be analyzed by the system claimed by VESTAL ET AL.

Claim 37 states: "A method of collecting a fluid sample for mass spectrometry analysis of multiple element content comprising the application of the sample to an inert matrix having a low background element content, wherein the matrix is selected from the group consisting of aragonite, aluminium hydroxide, titania, glucose, Starch "A", Starch "B", glucodin, cellulose powder/granules, fibrous cellulose, hydroxy butyl methyl cellulose, vegetable flour or mixtures thereof." The material claimed is taught in claim 61 of VESTAL ET AL. which states: "A method of analyzing a plurality of samples within a sample receiving chamber of a mass spectrometer, the method comprising: supporting each of a plurality of samples at a fixed location on one of a plurality of sample supports; identifying



each sample location of each of the plurality of samples on each of the plurality of sample supports; providing a vacuum lock chamber for receiving the sample supports and for maintaining one or more of the sample supports within a vacuum controlled environment while the plurality of samples on another of the sample supports are struck by laser pulses; automatically inputting and outputting each of the sample supports from the sample receiving chamber of the mass spectrometer to the vacuum lock chamber; striking each sample on each sample support while within the receiving chamber with a laser pulse to desorb and ionize sample molecules; and recording test data in a computer from the mass spectrometer for each of the plurality of samples on the sample support.”

As previously discussed with claim 1, claim 61 of VESTAL ET AL. also teaches the use of high energy radiation in the form of a laser pulses to ionize samples for analysis and the use of mass spectrometry for the analysis of samples. In addition, VESTAL ET AL. teaches that a sample can have a mixture of components for analysis as well as be unpurified before analysis, pages 9 – 10 of the Processing and Preparing Samples section. Also, VESTAL ET AL. teaches on page 1, lines 20 – 23 in the Background of the Invention section the use of the “appropriate matrix” for analysis which does not limit to particular type of matrix, but is dependent on the sample being analyzed.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 4 – 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over “Sugar additives for MALDI matrices improve signal allowing the smallest nucleotide change (A:T) in a DNA sequence to be resolved” by SHAHGHOLI ET AL. and “Structure of a Matrix Based on Polysaccharide Derivatives for the Immobilization of Biologically Active Substances” by BURKHANOVA ET AL.

As discussed in the 102(b) rejection above, SHAHGHOLI ET AL. teaches sugar additives, specifically glucose, for MALDI matrices (abstract) which are affixed to a support (page 3, column 2, lines 1-12).

SHAHGHOLI ET AL. does not teach a fibrous matrix or a fibrous matrix modified by oxidation and/or acid hydrolysis. However BURKHANOVA ET AL. teaches on page 488 “we took microcrystalline cellulose (MCC), obtained by acid hydrolysis from cotton cellulose, and U-type amylase” which meets the present limitations for the fibrous matrix of instant claim 4. It is the Examiner’s position the microcrystalline cellulose taught by BURKHANOVA ET AL. is in a different

physical form than the claimed fibrous cellulose but is chemically the same absent any evidence to the contrary.

With respect to claim 5, BURKHANOVA ET AL. further states "Chemical modification of the selected material was performed by specific oxidation with periodic acid and its salts." The previous and current statements show that BURKHANOVA ET AL. studied and used the modifying of cellulose by way of acid hydrolysis and oxidation.

It would have been obvious to one of ordinary skill in the art to use the matrices taught by BURKHANOVA ET AL., specifically fibrous cellulose or modified fibrous cellulose, in the sample collection device of SHAHGOLI ET AL. because of the ease of tailoring the cellulose to specific samples in enzymatic analyses (page 491, 5<sup>th</sup> paragraph).

### ***Conclusion***

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRYAN T. KILPATRICK whose telephone number is (571)270-5553. The examiner can normally be reached on Mon - Fri (alt Fri off); 7:30 am - 5:00 pm, 7:30 am - 4:00 pm (working Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on 571-272-1330. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BK

/Barbara L. Gilliam/  
Supervisory Patent Examiner, Art Unit 4128